UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/808,517	03/14/2001	William M. Sugden	960296.97982	4541

27114 7590 10/02/2002

QUARLES & BRADY LLP
411 E. WISCONSIN AVENUE, SUITE 2040
MILWAUKEE, WI 53202-4497

EXAMINER
WINKLER, ULRIKE

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/02/2002 06

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/808,517	Applicant(s) SUGDEN ET AL.	
	Examiner Ulrike Winkler, Ph.D.	Art Unit 1648	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 15-19 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 15-19 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Specification

The disclosure is objected to because of the following informalities: In the specification luciferase is referred to as "ranilla or renilla luciferase", for example see paragraph 0051, line 2 and paragraph 0055 line 11, this appears to be a typographical error. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, Paper No. 5, is attached to the instant Office Action.

Applicant is reminded, that listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Drawing

Formal drawings and/or photographs have been submitted which fail to comply with 37 CFR 1.84. Please see the form PTO-948.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES
A. Correction of Informalities -- 37 CFR 1.85

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, MUST be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings MUST be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in ABANDONMENT of the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15, 17 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 15 is not clear what is meant by "whereby an operable factor will link the sites". It is not clear if an additional step is intended with this phrase, i.e. a step ensuring that the factor present in the cell culture is able to link /loop the DNA sites, and this function would be considered "operable". What are the requirements of the factor to be considered "operable"?

In claim 15 it is not clear what is meant by "the candidate molecule inhibits protein:protein linking.....unable to mediate linking". What specifically is being linked? Does this refer to the dimerization of the liking factor itself? EBNA1 which is a protein binds DNA, the binding of the DNA sequences appears to be important for the activation of viral replication. The peptides disclosed (AA40-89 and AA 331-391) are able to inhibit DNA linking by EBNA1, each of the peptides also nonspecifically binds to DNA. It is not clear what protein:protein interactions are contemplated to achieve inhibition of viral replication. The assays provided in the specification (figure 3) indicates that the percentage of DNA linking goes down with an increase in the concentration of EBNA1 fragments, increase in the looping/linking factors.

Claim 15 lacks a resolution step or correlation step in the method that clearly relates the preamble to the method steps. The preamble indicates that the method is directed to screening for viral replication inhibitors. Yet the factor being analyzed in the final step (d) is the looping linking factor. There is no indication that if a particular result is observed such as that the factor is unable to mediate linking, that this result correlates with the inhibition of viral transcription or replication.

Claims 17 and 18 recite the limitation "the assay" spanning lines 1 and 2 of the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15, 16 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mackey et al. (Journal of Virology, 1995) in view of Becker et al. (Israel Journal of Medicine, 1972).

Due to the multiple interpretations possible, the office is interpreting the claims to be: The instant invention is drawn to a method of screening viral replication inhibitors and viral transcription inhibitors in a cell. The cell is contacted with the inhibitor and the viral transcription and translation is assayed. The assay also requires that a viral looping/linking factor is present in the cell and that that the nucleic acid that is being looped/linked comprises at least two binding sites for the factor. The factor binding sites are interpreted to be on the nucleic acid molecule in a plasmid. A plasmid by definition is a genetic element that is able to replicate independently of the host cell chromosome. The EBV viral DNA is interpreted as reading on a plasmid because the viral DNA is able to replicate independently of the host cell chromosome. Cells infected with EBV, Papilloma virus, Herpes Simplex virus or adenovirus all contain

looping/linking proteins as well as nucleic acids (plasmids) that comprise at least two binding sites for the factor.

Mackey et al. teach that multiple regions with EBNA1 can link DNA's. This DNA linking is determined using electrophoretic mobility shift assays. Mackey et al. established that high concentrations of EBNA1 would compete for the formation of linked complexes (see figure 1). The reference utilizes DNA molecules that comprise at least two EBNA1 binding sites (page 6201, column 2, lines 3-18). The reference assays the ability of EBNA1 to link DNA and found as the concentration of EBNA binding sites increased on the DNA this in turn increased the linking of DNA. With the addition of excess EBNA1 the DNA linking is decreased because of competition with the bound complexes. The reference measures the ability of a compound to form large DNA lattices, thereby measuring the ability of EBNA1 to link DNA, utilizing electrophoretic mobility shift assays. The reference does not assay for viral replication inside a cell.

Becker et al. disclose a cell-based assay to determine viral replication/inhibition, here Burkitt lymphoma cells that comprise EBV were tested for their ability to inhibit EBV DNA replication after treatment with distamycin. Burkitt lymphoma cells are latently infected with EBV and are positive for the presence of EBNA. Here the cells comprise DNA that contains more than one EBNA binding site as evidenced by the replication of the viral DNA. The cells are positive for EBNA indicating that they comprise a looping/linking factor. The reference teaches distamycin treated and untreated cells and compares the two cells for their EBV- DNA synthesis. The cells that were treated with distamycin did not replicate viral DNA indicating that distamycin is effective as an inhibitor for viral replication. The reference does not teach

analyzing the ability of the looping/linking factor to be inhibited by an excess of the looping/linking factor.

In the development of pharmaceuticals there is a natural progression that begins with an observation between molecules, first an inhibitor and a target are assayed in a test tube. Assays in a test tube format allow the artisan to precisely study the interaction between known molecules. Once an inhibitor of a particular reaction is established the next natural step would be to see if the inhibitor will function the same way inside a cell, should the inhibitor not work inside a cell this would be the end of the investigation because it would be unnecessary to further study the effect of the inhibitor in an *in vivo* animal model. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to assay the EBNA linking competitors as taught by Mackey et al. as potential inhibitors for EBV infection utilizing the EBV cell inhibition assay as taught by Becker et al. There was a high expectation of success in utilizing the whole cell assay methods for determining the viral replication inhibition. One having ordinary skill in the art would have been motivated to utilize the cell-based format of Becker et al. for the molecular format of Mackey et al. in the progression of developing better inhibitors for EBV infection. There is a great interest in developing inhibitors of EBV infection because immunosuppressed patients that are latently infected with EBV. Therefore, the instant invention over Mackey et al. in view of Becker et al.

Conclusion

No claims allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Feriotto et al. Binding of EBV nuclear antigen 1 to DNA inhibition by distamycin and two novel distamycin analogues. European Journal of Pharmacology (1994) Vol. 267, pp. 143-149.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 703-308-8294. The examiner can normally be reached M-F, 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 703-308-4027.

The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for informal communications use 703-308-4426.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ulrike Winkler, Ph.D. 9/26/01